

## **REMARKS**

The Office Action dated November 19, 2003, has been received and reviewed. Claims 1-7, 9-11 and 14-16 are pending in the present application and stand rejected. Claim 8 stands withdrawn by the Examiner in view of the restriction requirement. Applicants respectfully request reconsideration of the application in view of the claim amendments above and the remarks below.

### **I. Specification Objections**

Applicants note that a new declaration will be filed in response to Office Action as soon as Applicants' representative receives the corrected declaration. Applicants submit that this will be filed as soon as possible. Applicants have also amended the title and abstract of the present application as suggested by the Examiner. Applicants have also included a sequence listing with the present response as well as amended the specification to include the sequence identification language. Accordingly, Applicants respectfully request that the objections to the specification be withdrawn.

### **II. Claim Amendments**

Claims 1, 3-9, 11, 14 and 16 have been amended to clarify the claim language in view of the claim objections and to correct for changes from European to United States patent practice. Claim 2 has been amended into independent form. Accordingly, Applicants respectfully submit that the claims are now in condition for allowance.

### **III. Claim Objections**

Claims 2-9, 11 and 14 are objected to as allegedly containing informalities. Applicants have amended claims 3-9, 11 and 14 to begin with the word "The" rather than "A". Applicants submit that every claim can stand alone, and note by changing the word "a" to "the" in no way changes the scope of the present claims. Applicants have also included comma as indicated in the areas suggested by the Examiner. Applicants have also amended Claim 2 into independent form to better claim the subject matter of original Claim 2. Accordingly, Applicants respectfully request that the objections to the claims be withdrawn in view of the amendments.

#### **IV. Rejections under 35 U.S.C. § 112, first paragraph**

##### A. Enablement

Claims 1-8, 10-11 and 14-16 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse these rejections due to the amendments to the claims and the reasons enumerated below.

Applicants note that the "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (MPEP §2164.01, citing *In re Wands*, 858 F.2d 731, 737). Furthermore, the test for whether or not the enablement requirement has been met involves determining whether or not practice of the invention as claimed involves "undue experimentation". It has long been settled that "the key word is 'undue', not 'experimentation'". *In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976). In the present case, the references cited by the Examiner in the previous Office Action, taken together with the references cited by the Applicants in this reply show only that the application of the current technology requires routine effort, and not undue experimentation.

Applicants submit that the present application discloses various methods that can be employed to achieve high BiP levels in plants. Specifically, page 5, line 19 to page 16, line 18 lays out methods for increasing BiP levels. Additionally, the Examples illustrate increased BiP levels. Furthermore, WO94/08012 published 14 April 1994, which was cited in the International Search report, illustrates enablement for means of over expression of BiP. WO94/08012 relates to the state of the art of methods of increasing secretory protein synthesis, especially by over-expressed gene product(s). Furthermore, Applicants submit that well-known techniques in the art of plant breeding can be utilized to positively select a plant for desired characteristics to achieve high BiP levels in plants. Therefore, Applicants submit that the Claims 1-8, 10-11 and 14-16 are enabled.

The Claims also stand rejected to as allegedly the specification fails to provide guidance for exact hybridization or amplification conditions other than those for encoding tobacco BiP. Applicants have enclosed as Appendix I a list of other nucleic acids listing various species and kingdoms encoding BiP that were known at the time of the invention. Among plants, BiPs are extremely conserved (over 90% sequence similarity at protein level), between kingdoms it is less (70%) as reported in Denecke et al., 1991 a document referred to in the specification on page 3 line 16, page 22 line 27, page 25 line 2 and page 26 line 2. However, as noted in the specification and by one of skill in the art, it will be appreciated that it is the protein sequence and not the nucleotide sequence which is important for determining function. Genes code for proteins but it is the proteins which act. Accordingly it is the homology at the protein level that is relevant and not at the nucleotide level. It has been observed that because of the degeneracy of the genetic code, two genes encoding exactly the same protein may have less than 50% sequence homology at the nucleotide level. The 1991 Denecke et al. reference illustrated that tobacco BiP can complement the yeast BiP (a conditionally lethal BiP mutant could be made viable by expressing tobacco BiP). This demonstrates that the function of BiP is extremely conserved, even between kingdoms of organisms, and is the basis for the claim that the present invention would work with any BiP from any eukaryotic cell, **not just** tobacco BiP. Applicants further submit that "BiP activity" could be measured by an assay as reported in Leborgne-Castel, 1999. Accordingly, Applicants submit that the present application is enabled. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph to Claims 1-8, 10-11 and 14-16.

#### B. Written Description

Claims 1-7, 9-10 and 14-16 are also rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. Applicants respectfully disagree with this assertion.

Applicants note that the U.S.P.T.O. has clarified the standard for examining applications for compliance with respect to the written description requirement of 35 U.S.C. §112, first paragraph. These guidelines state, in part:

The examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed . . . .  
Consequently, rejection of an original claim for lack of written description should be rare.

(Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001); emphasis added). Applicants respectfully contend that the specification does provide a sufficient written description so that one skilled in the art would appreciate that the Applicant was in possession of the claimed invention at the time of filing.

As noted above, Applicants have enclosed as Appendix 1, a list of other nucleic acids across species and kingdoms encoding BiP that were known at the time of the invention. The 1991 Denecke et al. reference cited to in the present application illustrates the highly conserved nature of BiP thus illustrating the broad range of nucleic acids that could be used in accordance with Claims 1-7, 9-10 and 14-16 of the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph to Claims 1-7, 9-10 and 14-16.

#### **V. Rejections under 35 U.S.C. § 112, second paragraph**

Claims 1-7, 9-11 and 14-16 are rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejections in view of the claim amendments and the following remarks.

Claim 1 stands rejected to as allegedly being indefinite. Applicants have amended Claim 1 to recite "maintaining" and removing reference to "causing". Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claim 1.

Claims 1, 3-7, 10-11 and 14-16 stand rejected as allegedly being indefinite in their recitation of "homologue". Applicants note that on page 6 lines 11 to 12 it is stated: "For the purposes of this patent application the term BiP includes any homologue thereof which has a significant degree of structural or functional similarity". Accordingly, Applicants submit that the

term homologue is defined in the specification and therefore request that the rejections to Claims 1, 3-7, 10-11 and 14-16 be withdrawn.

Claims 5-7 stand rejected as it is allegedly unclear what the meaning of containing is. Applicants have amended containing to read comprising as suggested by the Examiner. Accordingly, Applicants submit that these claims are now in condition for allowance.

Claims 5-7 also stand rejected as allegedly being indefinite in their recitation of "3' untranslated end" and "stop sequence". Applicants have amended these claims to recite "3' untranslated region" and "stop codon". Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claims 5-7.

Finally, Claim 16 stands rejected as allegedly being indefinite in its recitation of "in an amount sufficient to protect the plant". Applicants have added the recitations "in an amount sufficient to accelerate the induction of PR gene expression" to Claim 16. Support for this recitation can be found on page 18 lines 16 to 18. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claim 16.

## **VI. Rejections under 35 U.S.C. § 102(b)**

### A. Crofts et al.

Claims 1-2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Crofts et al., (1998) *Plant Cell* 10:813-823. Applicants respectfully traverse this rejection for the reasons set forth below.

Case law holds and the M.P.E.P. states that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Additionally, anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000).

Applicants note that prior to December 15, 1998, the earliest priority date of the present application, BiP or other ER chaperones are induced **during** plant pathogen as a **consequence** of high secretory protein synthesis. Again, prior to this date there was no disclosure that BiP over-

expression could **lead to resistance**, and BiP had never before been considered as a pathogenesis related protein (PR). The present application illustrates that BiP is induced **prior** to PR proteins. *See*, page 4 lines 6 to 16. The present application also illustrates that BiP over-expression leads to accelerated PR gene induction at the transcriptional level. Accordingly, this means the defense response is accelerated leading to the claims recited in the present application.

Applicants further note that one of the present inventors, Jurgen Denecke, is a co-author of the Crofts et al. citation, and note that this citation discloses plants transformed with a nucleic acid encoding BiP and plants overproducing calreticulin. However, Crofts et al. does not specifically disclose or teach plants with increased pathogen resistance. Instead, Crofts et al. on page 821 column 1 lines 5 to 8 states that "it is important to conduct further research to elucidate the function of this novel complex". Thus, Crofts et al. merely identifies a complex, but is unable to provide a function for it such complex, because Crofts et al. it fails to appreciate the link between increased pathogen resistance and increased BiP levels. Accordingly, as recited in Claim 1, a method to increase secretory protein synthesis, and a method of reducing the period of time for responding to a pathogen attack in Claim 2 is not disclosed either explicitly or implicitly in the Crofts et al. Therefore, Applicants respectfully request reconsideration and withdrawal to the 35 U.S.C. § 102(b) rejections to Claims 1 and 2.

B. Arora et al.

Claims 1-4, 10-11 and 14-15 stand rejected as allegedly being anticipated by Arora et al. (1998) *Physiol. Planta.* 103: 24-34. Applicants respectfully disagree with this assertion. Applicants submit that Arora et al. discloses the observation that BiP accumulates in water stressed tissues of geranium plants and that tissue that is water stressed is more heat tolerant. There is no mention of a method of increasing secretory protein synthesis by causing a plant to maintain a level of BiP greater than the endogenous level under non-stressful conditions. Accordingly, independent Claims 1 and 2 and their subsequent dependent claims are not anticipated with respect to Arora et al. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejections to Claims 1-4, 10-11 and 14-15.

C. Zhang et al.

Claims 1-4, 10-11 and 14-15 also stand rejected as allegedly being anticipated by Zhang et al., (1992) *Protoplasma* 171: 142-152. Applicants respectfully disagree with this assertion. Applicants submit that Zhang et al. discloses maize mutant plants in which BiP levels are elevated. Zhang et al. Note that the elevation of BiP level is not thought to be as a result of a mutation in the BiP gene itself but rather as a result of stress. See, page 150, column 2, 2<sup>nd</sup> paragraph. Zhang et al. does not disclose a method to increase secretory protein synthesis nor a method of reducing the period of time for responding to a pathogen attack. Indeed, Zhang et al. is silent with respect to pathogens. Accordingly, Applicants submit that Claim 1-4, 10-11 and 14-15 are not anticipated by Zhang et al. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejections to Claims 1-4, 10-11 and 14-15.

**VII. Rejections under 35 U.S.C. § 103(a)**

A. Claims 1-7, 10-11 and 14-15

Claims 1-7, 10-11 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Crofts et al., (1998) *Plant Cell* 10:813-823. Applicants traverse this rejection for the reasons set forth below and the reasons discussed above in the 102(b) section.

To establish a prima facie case of obviousness, the prior art reference or references when combined must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55

U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as recently affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual question of motivation is material to patentability, **and cannot be resolved on subjective belief and unknown authority**. See *In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a prima facie showing of obviousness under § 103.

Applicants re-emphasize that BiP acts as a "trigger" to accelerate pathogen resistance and not merely as a consequence of a pathogen challenge. This is corroborated by the data in Figures 11 and 12 and in Examples 12 and 13 of the application. Applicants submit that Crofts et al. does not teach or suggest the constructs used to transform the plants and the levels of BiP produced in the present invention. The methods disclosed by Crofts et al. refer to a method by N. Leborgne-Castel and J. Denecke for teaching transgenic plant that overexpress BiP. See, *Plant Cell*, (1999) 11(3): 459-70. The N. Leborgne-Castel and J. Denecke paper was not published until March 1999, i.e., after the earliest priority date of the present application. Therefore, not only is Crofts et al. not enabling, but there is no suggestion or motivation to modify the teachings of Croft et al. to arrive at the present invention as claimed in Claims 1-7, 10-11 and 14-15. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejections to Claims 1-7, 10-11 and 14-15.

#### B. Claims 9 and 16

Claims 9 and 16 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Crofts et al. in combination with Denecke et al. (1995) *Plant Cell* 7: 391-406. Applicants respectfully disagree with this assertion. Applicants note that it is alleged that Denecke et al. teaches that levels of BiP are increased in **response** to salicylic acid, and that one of ordinary skill in the art would have been motivated to increase the expression of BiP in plants with SA. However, as previously mentioned Crofts et al. is not enabling for the present claims and there is no motivation to combine Crofts et al. with Denecke et al. because Crofts et al. is concerned with the function of the BiP-calreticulin complex and not pathogen resistance. Applicants submit that the combination of these documents would not lead to Claims 9 and 16 as one of ordinary skill in the art would not have been able to develop plant resistance by a mere combination of these documents. As in *In re Sang-su Lee*, a factual question of motivation is material to patentability,



and cannot be resolved on subjective belief and unknown authority. Accordingly, Applicants submit that the combination of Crofts et al. and Denecke et al. does not teach or suggest the elements of Claims 9 and 16 of the present application.

C. Claims 1-4, 6, 10, 11, 14 and 15

Claims 1-4, 6, 10, 11, 14 and 15 also stand rejected as allegedly being unpatentable in view of Coughlan et al., U.S. Patent No. 6,171,864. Applicants respectfully disagree with this assertion. The '864 patent discloses novel compositions for calreticulin and calnexin proteins, genomic sequences, and promoters as well as uses of these proteins and sequences in controlling expression of resistance genes. It further discloses plant cells transformed with a vector encoding calreticulin, which it is believed would increase the levels of BiP in the plant over endogenous levels. However, the '864 patent merely acknowledges that BiP is one of an array of chaperones and does not disclose plants transformed with a vector encoding calreticulin. Applicants submit that there is no suggestion or motivation to modify the teachings of this reference or to combine it with any other citation to the presently claimed methods of increasing secretory protein synthesis or reducing the period of time for responding to a pathogen attack. Accordingly, Applicants submit that the '864 patent does not teach or suggest all of the elements of Claims 1-4, 6, 10, 11, 14 and 15. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejections to Claims 1-4, 6, 10, 11, 14 and 15.

**CONCLUSION**

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

Applicants have included a one-month extension of time fee with this response. It is believed that no other fees and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees

In re: Denecke et al.  
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Filed: June 15, 2001  
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believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,



Jarett K. Abramson  
Registration No. 47,376

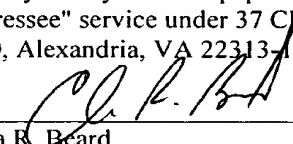
**USPTO Customer No.: 20792**  
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Date of Deposit: March 19, 2004

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Clara R. Beard

## Appendix I

### Non-plant BiPs published before filing in December 1998

#### *Saccharomyces cerevisiae* (Yeast)

Rose MD, Misra LM, Vogel JP.

KAR2, a karyogamy gene, is the yeast homolog of the mammalian BiP/GRP78 gene. Cell. 1989 Jun 30;57(7):1211-21.

mffnrlsagk llvplsvvly alfvvilplq nsfhssnvlv

41 rgaddvenyg tvigidlgtt yscvavmkng kteilaneqg  
81 nritpsyvaf tdderligda aknqvaanpq ntifdikrli  
121 glkyndrsvq kdikhlpfnv vnkdgkpave vsvkgekkvf  
161 tpeeisgmil gkmkqiaedy lgtkvthavv tpayfndaq  
201 rqatkdagti aglnvlrvn eptaaaiayg ldkdskehqi  
241 ivydlgggtf dvslisieng vfevqatsgd thlggedfdy  
281 kivrqlikaf kkkhgidvds nnkalaklkr eaekakrals  
321 sqmstrieid sfvdgidlse tltrakfeel nldlfkktlk  
361 pvekvldsg lekdvddiv lvggstripk vqqllesyfd  
401 gkkaskginp deavaygaav qagvlsgeeg vedivldvn  
441 altlgiettg gvmtplikm taipkksqi fstavdnqpt  
481 vmikvyeger amskdnllg kfeltgippa prgvpqievt  
521 faldangilk vsatdkgtgk sesititndk grltqeeidr  
561 mveeaekfas edasikakve smklenyah slknqvngdl  
601 gekleedke tlldaandvl ewlddnfeta iaedfdekfe  
641 slskvaypit sklyggadgs gaadyddede dddgdyfeh  
681 el

#### *Aspergillus* (mold)

Hijarrubia, M. J., Casqueiro, J., Gutierrez, S., Fernandez, F. J., and Martin, J. F. Characterization of the bip gene of *Aspergillus awamori* encoding a protein with an HDEL retention signal homologous to the mammalian BiP involved in polypeptide secretion. Curr Genet 32, 139-46 (1997).

marishqgaa kpftawttif ylllvfiapl affgtahaqd

41 etspqesygt vigidlgty scvgvmqngk veilvndqgn  
81 ritpsyvaf deerlvгда knqyaanpr r tifikrlig  
121 rkfdkdvqk dakhfpykv nkdgkphkv dvnqtpklt  
161 peevsamvlg kmkeiaegyl gkkvthavvt vpayfndaqr  
201 qatkdagtia glnvlrvne ptaaiaygl dktgderqvi  
241 vydlgggtfd vsllsidngv fevlatagdt hlgedfdqr  
281 vmdhfvklyn kknvvdvtd lkamgklkre vekakrtlss  
321 qmstrieiea fhngedfset ltrakfeeln mdlfkktlkp  
361 veqvlkdakv kksevddivl vggstripkv qalleeffgg  
401 kkaskginpd eavafgaavq ggvlsggegt gdvvlmdvnp  
441 ltlgiettg vmtkliprnt viptrksqif staadnqptv  
481 liqvyegers ltkdnllgk feltgippap rgvpqievsv  
521 dldangillkv hasdkgtgka esititndkg rlsqeeidrm  
561 vaeaeefae dkaikakiea mtlenyafs lknqvndeng  
601 lggqideddk qtildavkev tewlednaat attedfeeck  
641 eqlsnvaypi tsklygsapa deddepsghd el

### Nematode worm

Wilson,R.

Genome sequence of the nematode *C. elegans*: a platform for investigating biology. The *C. elegans* Sequencing Consortium  
JOURNAL Science 282 (5396), 2012-2018 (1998)

mktlflgli alsavsvyce eeektekket kygtiigidl gttyscvgy kngrveiian

61 dqgnritpsy vafsgdqgdr ligdaaknql tinpentifd akrigrdyn dktvqadikh  
121 wpfkvidksn kpsvevkvs dnkqftpeev samvlvkmke iaesylgkev knavvtvpay  
181 fndaqrqatk dagtiaglnv vriineptaa aiaygldkkd gernilvfdl gggtfdvsmi  
241 tidngvfevl atngdthlgg edfdqrvmey fiklykkksg kdlrkdkrav qklrreveka  
301 kralstqhqt kveieslfdg edfsetltra kfeelnmdlf ratlkipvqkv ledsdlkkdd  
361 vheivlviggs tripkvqqli keffngkeps rginpdeava ygaavqggvi sgeedtgeiv  
421 lldvnpitmg ietvggvmk ligrntvipt kksqvfstaa dnqptvtiqv fegerpmtkd  
481 nhqlgkfdlt glppaprgvp qievtfeidv ngilhvtad kgtgnknkit itndqnrlsp  
541 edierminda ekfaeddkkv kdkaeamel esyaynlknq iedkeklggk ldeddkktie  
601 eaveeaiswl gsnaeasae lkeqkkdles kvqipvskly kdagaggeea peegsddkde  
661 l

### Chicken

Stoeckle,M.Y., Sugano,S., Hampe,A., Vashistha,A., Pellman,D. and Hanafusa,H.

78-kilodalton glucose-regulated protein is induced in Rous sarcoma virus-transformed cells independently of glucose deprivation  
Mol. Cell. Biol. 8 (7), 2675-2680 (1988)

1 mrhlallll lggaraddee kkedvgtvvg idlgttyscv gvfkngrvei iandqgnrit  
61 psyvaftpeg erligdaakn qltsnpentv fdakrligt wndpsvqqdi kylpfkvvek  
121 kakphiqv dv gggqtktfap eeisamvltk mketaeaylg kvvthavtv payfndaqrq  
181 atkdagtiag lnmriinep taaaiaygld kregekniv fdlgggtdv sltidngvf  
241 evvatngdth lggedfdqrv mehfiklykk ktgkdvrkdn ravqklrrev ekakralssq  
301 hqarieiesf fegedfsetl trakfeelnm dlfrstmkpv qkvledsdlk ksdideivlv  
361 ggstripkiq qlvkeffngk epsrginpde avaygaavqa gvlsqdqdtg dlvlldvcpl  
421 tlgietvggv mtklipmtv vptkksqifs tasdnqptvt ikvyegerpl tkdnhllgtf  
481 dltgippapr gvpqievtfe idvngilrvt aedkgtgnkn kititndqnr ltpieermv  
541 ndaekfaeed kklkeridar nelesyaysl knqigdkekl ggklssedke tiekaveeki  
601 ewleshqdad iedfksskkke leevvpivs klygsagppp tgeeeaaekd el

### Chinese Hamster

Ting,J., Wooden,S.K., Kriz,R., Kelleher,K., Kaufman,R.J. and Lee,A.S.

The nucleotide sequence encoding the hamster 78-kDa glucose-regulated protein (GRP78) and its conservation between hamster and rat

Gene 55 (1), 147-152 (1987)

1 mkfpmvaaa lllcavraee edkkedvgtv vgidlgttys cvgvfkngrv eiiandqgnr  
61 itpsyvaft egerligdaa knqltsnpen tvfdakrlig rtwndpsvqq dikflpfkvv  
121 ekktkpyiqv digggqtktf apeesamvl tkmketaeay lgkkvthavv tvpayfndaq  
181 rqtakdagti aglnvmriin eptaaaiayg ldkregekni lvfdlggtf dvsltidng

241 vfevvatngd thlggedfdq rvmehfikly kkkktgkdvrk dnravqklrr evekakrals  
 301 sqhqarieie sffegedfse tltrakfeel nmdlfrstmk pvqkvledsd lkksdideiv  
 361 lvvgstripk iqqlvkeffn gkepsrginp deavaygaav qagvlsqdq dtgdlvldvc  
 421 pltlgietvg gvmtnklipr tvvptkksqi fstasdnqpt vtikvyeger pltkdnhlhg  
 481 tfdltgippa prgvpqiev tfeidvngilr vtaedkgtgn knkititndq nrltpeeier  
 541 mvndaekfae edkklkerid tmelesyay slknqigdke klggklssed ketmekavee  
 601 kiewleshqd adiedfkakk keleeivqpi isklygsagp pptgeedtse kdel

#### Mouse

Kozutsumi, Y., Normington, K., Press, E., Slaughter, C., Sambrook, J.  
 and Gething, M.J.

Identification of immunoglobulin heavy chain binding protein as  
 glucose-regulated protein 78 on the basis of amino acid sequence,  
 immunological cross-reactivity, and functional activity  
 J. Cell Sci. Suppl. 11, 115-137 (1989)

mmkftvvaaa lllgavrae eedkkedvgt vvgidlgty scvgvfkngv veiiandqgn  
 61 ritpsyvaft pegerligda aknqltsnpe ntvfdakrli grtwndpsvq qdikflpfkv  
 121 vekktkpyiq vdigggqtk fapeeisamv ltkmketaea ylgkkvthav vtvpayfnda  
 181 qrqatkdaqt iaglnvmrri neptaaaiay gldkregekn ilvfdlggt fdvslitdn  
 241 gvfevvatng dthlggedfd qvmehfikl ykkktgkdvr kdnravqklr revekakral  
 301 ssqhqariei esffegedfs etltrakee lnmldfrstm kpvqkvleds dlkksdidei  
 361 vlvgstrip kiqqlvkeff ngkepsrgin pdeavaygaa vqagvlsqdq dtgdlvldvc  
 421 cpltlgietv ggvmtnklipr ntvvptkksq ifstasdnqp tvtikvyege rpltkdnhlh  
 481 gtfdltgipp aprgvpqiev tfeidvngil rytaedkgtg nknkititnd qnrltpeeie  
 541 rmvndaekfa eedkklkeri dtmelesya yslknqigdk eklggklssed dketmekave  
 601 ekiewleshq dadiedfkak kkeleeivqp iisklysgg ppptgeedts ekdel

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#### A selection of plant BiP sequences published before filing in December 1998

Tobacco BiP in 1991, you have this references and it cites 8 isoforms of tobacco BiP,  
 which could mean that there are 8 or more isoforms in tobacco. The patent is based on  
 isoform 4 (BLP4), but the other isoforms are over 90% identical

#### Arabidopsis thaliana

Koizumi, N.

Isolation and responses to stress of a gene that encodes a luminal binding protein in  
 Arabidopsis thaliana

Plant Cell Physiol. 1996

Volume 37

862-865

#### Soybean

Figueiredo, J.E.F., Cascardo, J.M., Carolino, S.M.B., Alvin, F. and  
 Fontes, E.P.B.

Water-stress regulation and molecular analysis of the soybean BIP

gene family  
Braz. J. Plant Physiol. 9, 103-110 (1997)

#### **Rice**

Muench,D.G., Wu,Y., Zhang,Y., Li,X., Boston,R.S. and Okita,T.W.  
Molecular cloning, expression and subcellular localization of a BiP  
homolog from rice endosperm tissue  
Plant Cell Physiol. 38 (4), 404-412 (1997)

#### **Maize**

Wrobel,R.L., O'Brian,G.R. and Boston,R.S.  
Comparative analysis of BiP gene expression in maize endosperm  
Gene 204 (1-2), 105-113 (1997)

#### **Spinach**

Anderson,J.V., Neven,L.G., Li,Q.B., Haskell,D.W. and Guy,C.L.  
A cDNA encoding the endoplasmic reticulum-luminal heat-shock  
protein from spinach (*Spinacia oleracea* L.)  
Plant Physiol. 104 (1), 303-304 (1994)

#### **Tobacco BLP4 (one of 8 cloned isoforms, there could be more than 8)**

maggawnrrt slivfgivlf gclfafsiat eeatklgtvi gidlgttysc vgvyknghve  
61 liandqgnri tpswvaftdg erligeaakn laavnpertv fdvkrigrk fddkevqrdm  
121 klvpykivnk dgkpyiqvki kdgetkifsp eeisamiltk mketaeaylg kkikdavvtv  
181 payfndaqrq atkdagviag lnvariinep taaaiaygld kkggekniltv fdlgggtfdv  
241 siltidngvf evlstngdth lggedfdqri meyfikklikk khgkdiskdn ralglrrea  
301 erakralssq hqvrveiesl fdgvdfsepl trarfeelnn dlfrktmgpv kkamddagle  
361 ktqideivlv ggstripkvq qlldkdyfdgk epnkgvnpde avaygaavqg gilsgeggde  
421 tkdillldva pltlgietvg gvmtkliprn tviptkksqv ftyqdqqt vtiqvfege  
481 sltkdcrllg kfdltgiapa prgtpqievt fevdangiln vkaedkasgk sekititndk  
541 grlsqeeier mvkeaeefae edkkvkerid arnsletyvy nmrmqindkd kladklesde  
601 kekietatke alewlddnqs aekedyekl keveavcnpi itavyqksgg apggesgase  
661 dddhdel

#### **Arabidopsis thaliana (one of three isoforms in this species)**

marsfganst vvlaiiffgc lfafstakee atklgsvigi dlgttyscvg vyknghveii  
61 andqgnritp swvgftdser ligeaaknqa avnpertvfd vkrigrkfe dkevqkdrkl  
121 vpyqivnkdg kpyiqvkikd getkvfspee isamiltkmk etaeaylgkk ikdavvtvpa  
181 yfndaqrqat kdagviagln variinepta aaiaygldkk ggekniltvfd lgggtfdvsv  
241 ltidngvfev lstngdthlg gedfdhrime yfiklikkkh qkdiskdnka lgklrrecer  
301 akralsqhq vrveieslfd gvdlsepltr arfeelnndl frktmgpvkk amddaglkqs  
361 qideivlvvg stripkvqql lkdfegkep nkgvnpdeav aygaavqggi lsgeggdetk  
421 dillldvapl tlgtietvgv mtklipmntv iptkksqvft tyqdqqtvs iqvfegersl  
481 tkdcsllgkf dlgtgvppapr gtpqievtfe vdangilnvk aedkasgkse kititnekgr  
541 lsqeeidrmv keaeefaeed kkvkekidar naletyvynm knqvskdkl adklegdeke  
601 kieaatkeal ewldenqnse keeydeklke veavcnpiit avyqrggap gaggesstee  
661 edeshdel

### Glycine max

magswarrsl ivlaiisfgc lfaisiakee atklgtvigi dlttyscvg vykngheii

61 annqgnritp swvaftdser ligeaaknla avnpertifd vkrigrkfe dkevqrdmkl  
121 vpykivnkdg kpyiqvkikd getkvfspee isamiltkmk etaeafgkk indavvtvpa  
181 yfndaqrqat kdagviagln variinepta aaiaygldkk ggeknilvfd lgggtfdvsi  
241 ltidngvfev latngdthlg gedfgqrime yfiklikkkh gdiskdnra lgklrreaer  
301 akralsqhq vrveieslfd gvdfepltr arfeelnndl frktmgpvkk amedaglkqs  
361 qideivlvvg stripkvqql lkdyfdgkep nkgvnpdeav aygaavqegi lsgeggeetk  
421 dillldvapl tlgietvggv mtklipmtv iptkksqvft tyqdqqtvs iqvfegersl  
481 tkdcrllgkf dlsgippapr gtaqievtfe vdangilnvk aedkgtgkse kititnekgr  
541 lsqeeierv reekdfaeek kvkeridar nsletyvynm knqvsdkdkl adklesdeke  
601 kietavkeal ewlddnqsme kedyeklkve veavcnpiis avyqrsaggp ggggasgeed  
661 eddshdel

### Rice

mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian

61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rdigrkfeek evqrdmklvp  
121 ykivnkigkp yiqvkikdge nkvspeevs amilgkmket aeaylgkkin davvtvpayf  
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkkg eknilvfdlg ggtfdvsilt  
241 idngvfevla tngdthlgge dfdqrimyef iklikkkysk diskdnralg klrreaerak  
301 ralsnqhqr veieslfdgt dfsepltrar feelnndlfr ktmgvpkkam ddagleksqi  
361 heivlvvggst ripkvqqlr dyfegkepnk gvnnpdeavay gaavqgsils geggdetkdi  
421 lldvapltil gietvggvmnt klipmtvip tkksqvftty qdqqttsiq vfegersmtk  
481 dcrllgkfdl sgipaaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls  
541 qeeidrmvre aeefaeedkk vkeridarnq letyvynmkn tvgdkdklad kleseekekv  
601 eealkealew ldenqtaeke eyeeklkve avcnpiisav yqrtggaggp mrrgrlddeh  
661 del

### Maize

mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian

61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rigrkfqdk evqrdmklvp  
121 ykiinkdgp yiqvkikdge nkvspeeis amilgkmkdt aeaylgkkin davvtvpayf  
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkkg eknilvfdlg ggtfdvsilt  
241 idngvfevla tngdthlgge dfdqrimyef iklikkkysk diskdnralg klrreaerak  
301 ralsnqhqr veieslfdgt dfsepltrar feelnndlfr ktmgvpkkam edagleksqi  
361 heivlvvggst ripkvqqlk dyfngkepnk gvnnpdeavaf gaavqgsils geggdetkdi  
421 lldvapltil gietvggvmnt klipmtvip tkksqvftty qdqqttsiq vfegersmtk  
481 dcrllgkfdl ngipsaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls  
541 qeeidrmvre aeefaeedkk vkeridarnq letyvynmkn tvgdkdklad kleaeekv  
601 eealkealew lddnqsaeke dyeeklkve avcnpivsav yqrsaggagg dadggvdddh  
661 del

### Spinach

mavawksras siafgivllg slfafsakd eapklgtvig idlttyscvg gvykdgkvei

61 iandqgnrit pswvaftnde rligeaaknq aanpertif dvkrigrkf edkevqkdmk  
121 lvykivnrd gkpyiqkvq egetkvfspe eisamiltkm ketaetflgk kkdavvtvp

181 ayfndaqrqa tkdagviagl nvariinept aaaiaygldk rggeknilvf dlgggtfdvs  
241 vltidngvfe vlatngdthl ggedfdqrlm eyfiklikkk htkdiskdnr algklrrece  
301 rakralssqh qvrveieslf dgvdseplf rarfeelnnd lfrktmgpvk kamddaglek  
361 nqideivlvq gstripkvqq llkeffngke pskgvnpdea vafgaavqgs ilsgeggeet  
421 keillldvap ltlgietvvg vmtklipmt viptkksqvf ttyqdqqtiv tiqvfevers  
481 ltkdcrllgk fdlgtiapap rgtpqievtf evdangilnv kaedkasgks ekititndkg  
541 rlsqeeierm vreaeefae dkkvkekida mnsletyyn mknqisdadk ladvlesdek  
601 ekiegavkea lewlddnqsa ekedydeklk eveavcnpii tavyqrsggp sgesgadsed  
661 seeghdel